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Syphilitic hepatitis as a manifestation of secondary syphilis

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ABSTRACT

Syphilis is a multisystem disease caused by the spirochete *Treponema pallidum*. Among various organs affected, liver involvement is seen infrequently and can be missed. Here we present a case of hepatitis due to secondary syphilis that completely resolved with penicillin G therapy.

KEYWORDS Penicillin; rash; syphilis

Infection with the spirochete *Treponema palladium* can involve virtually any organ of the body but is uncommon in the liver, with syphilitic hepatitis occurring in 0.2% to 3% of patients with syphilis.[1] *T. palladium* is one of the nonhepatotropic pathogens usually associated with mild liver injury and can therefore be missed.[2]

CASE DESCRIPTION

A 55-year-old man with a history of unprotected sex with men presented with night sweats and a rash on the chest, arms, and palms for 4 months. He did not have any known liver disease and his liver function tests were normal 3 months earlier. He denied any alcohol intake, recent acetaminophen use, herbal product use, or recreational drug use. His only medication was emtricitabine-tenofovir for preexposure prophylaxis for HIV. He was afebrile with a normal blood pressure and heart rate. He was alert, oriented, and anicteric and the abdomen was soft and nontender with normal bowel sounds. The liver and spleen were not palpable. Lymphadenopathy was absent. No precordial murmur was present. He had a nonitchy, erythematous, maculopapular rash in the chest, arms, and palms. No genital lesions were present. The aspartate aminotransferase was 70 U/L, alanine aminotransferase 148 U/L, alkaline phosphatase 442 U/L, gamma-glutamyl transferase 347 U/L, total bilirubin 0.8 mg/dL, and direct bilirubin 0.2 mg/dL. The blood count profile was normal.

Serology tests for hepatitis A, B, C, and E viruses were negative. An HIV test was negative. Autoimmune serology revealed negative antinuclear antibody, antimitochondrial antibody, and anti-LKM antibody titers. Anti–smooth muscle antibody titer was weakly positive (1:80). IgG subclass analysis was normal. Ferritin was normal with transferrin saturation of 14.4%. Serum copper was 188 mcg/dL with normal ceruloplasmin level.

A computed tomographic scan of abdomen and pelvis with contrast showed multiple, 2- to 5-mm low-density hepatic nodules. The liver measured 16 cm cephalocaudally and the spleen was unremarkable. A rapid plasma reagin test was positive at a titer of 1:64. He was treated with a single dose of 2.4 million units intramuscular penicillin G followed by resolution of skin rash and other systemic symptoms along with return of laboratory parameters including liver function tests to normal in 6 months. An anti–smooth muscle antibody titer repeated after treatment was negative. A repeat HIV test was negative. A computed tomographic scan of his abdomen after treatment showed normal liver parenchyma with resolution of the previously seen hypodensities. Laboratory results including liver function tests are summarized in *Table 1*.

DISCUSSION

Syphilitic hepatitis was first described by Harn in 1943.[3] Diagnostic criteria for syphilitic hepatitis were established by Mullick et al[4] in 2004 and include (1) abnormal liver enzymes

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Table 1. Laboratory values at baseline, pretreatment, and posttreatment

Lab parameter	Baseline	Pretreatment	Posttreatment
Aspartate aminotransferase (U/L)	21	70	20
Alanine aminotransferase (U/L)	49	148	43
Alkaline phosphatase (U/L)	91	442	97
Total bilirubin (mg/dL)	0.7	0.8	0.7
Direct bilirubin (mg/dL)	0.2	0.2	0.2
Albumin (g/dL)	4.1	3.4	4.5
International normalized ratio	—	1.1	—
Gamma-glutamyl transpeptidase (U/L)	—	347	42
Rapid plasma reagin (titer)	Nonreactive	1:64	Nonreactive

indicating liver involvement, (2) serological evidence of syphilis, (3) exclusion of alternative causes of liver diseases, and (4) improvement in liver enzymes following appropriate antimicrobial therapy. Our case met all four diagnostic criteria.

Clinical features of syphilitic hepatitis can be very nonspecific and can be related to hepatic or other organ system involvement. Our patient presented with rashes and night sweats. Other systemic symptoms can include fever, abdominal pain, jaundice, poor appetite, sore throat, phallodynia, headache, weight loss, arthralgia, myalgia, and lymphadenopathy among others. The typical laboratory abnormalities of syphilitic hepatitis will show elevated liver enzymes with a marked increase in alkaline phosphatase and gamma-glutamyl transpeptidase and a mild increase in aspartate aminotransferase or alanine aminotransferase levels. Physical examination findings can include hepatomegaly, splenomegaly, lymphadenopathy, and uveitis.[5]

Hepatic lesions can include granulomas, which are typical of syphilitic hepatitis.[2] *T. palladium* can be identified in the liver biopsy by immunohistochemical staining or silver stain.[6] Penicillin is the first-line treatment for syphilis, and response to therapy is one of the diagnostic criteria.[4] Identification and timely treatment of syphilitic hepatitis is crucial, because it can progress to fulminant hepatic failure in the absence of treatment.[7]

Although higher-income countries have a decreasing prevalence of syphilis in heterosexual men and women, the resurgence of syphilis in men who have sex with men has been noted.[5] Syphilis should be on the differential list in those with high-risk sexual behavior.

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